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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DUFFY, BRADLEY	
ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
03/16/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/589,450	PETERS ET AL.	
	Examiner	Art Unit	
	BRADLEY DUFFY	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,18-20 and 23-25* is/are pending in the application.

4a) Of the above claim(s) *10,11 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,18-20,23 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/24/11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 17, 2009, has been entered.

2. The amendment filed November 17, 2009, is acknowledged and has been entered. Claims 1-6, 9 and 18-20 have been amended. Claims 26 and 27 have been canceled.

3. Claims 1-11, 18-20 and 23-25 are pending in the application.

4. Claims 10-11 and 25 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant elected without traverse in the reply filed October 14, 2008.

5. Claims 1-9, 18-20, 23 and 24 are under examination. The elected invention is drawn to a method of treating colon cancer in a human patient by administering to said patient a human immunoglobulin specifically binding to the human EpCAM antigen, said immunoglobulin exhibiting a serum half-life of at least 15 days, said method comprising the step of administering said immunoglobulin no more frequently than once every week.

Information Disclosure Statement

6. The references cited in the information disclosure statement filed on January 24,

2011, have been considered.

Grounds of Objection and Rejection Withdrawn

7. Unless specifically reiterated below, Applicant's amendment and/or arguments filed November 17, 2009, have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed July 17, 2009. Notably, Applicant's amendment of the claims has rendered moot the previous 103(a) rejection. However, in order to promote compact prosecution, Applicant's arguments and Dr. Prang-Richard's 1.132 declaration will be addressed as relevant to the new 103(a) rejection set forth below.

Grounds of Objection Maintained

Oath/Declaration

8. The objection to the declaration is maintained.

In the reply filed November 17, 2009, Applicant submits that a new declaration has been provided.

In response a new declaration could not be found in the November 17, 2009 filing.

Accordingly a new oath or declaration in compliance with 37 CFR 1.63 including the entire inventive entity remains required. See MPEP 201.03, 605.04 and 37 CFR 1.63.

In order to obviate this issue it is suggested that the pages of the new oath recite page 1 of 3, page 2 of 3 and page 3 of 3, respectively.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-9, 18-20, 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kufer et al (WO 98/46645 A2, 1998, of record), in view of Raum et al (Can. Immunol. Immunother., 50:141-150, 2001, of record), in view of Naundorf et al (Int. J. Can. 100:101-110, 2002, of record), in view of Korman et al (US 20020086014

A1, 2002), in view of Wolf et al (DDT., 7(5):S25-S27, 2002, of record), in view of Raun et al (Neoplasia, 5(6):489-94, 2003, IDS filed 1/24/2011) and in view of Leyland-Jones (J. Clin. Onc., 221(21):3965-3971, 2003, of record).

As drawn to the elected invention and as currently amended, the claims are herein drawn to methods of treating colon cancer with EpCAM expression elevated relative to healthy colon tissue in a human patient comprising administering to said patient a human antibody comprising a heavy chain with the amino acid sequence of SEQ ID NO: 1 and a light chain with the amino acid sequence of SEQ ID NO: 2, wherein the antibody specifically binds to the human EpCAM antigen, said method comprising the step of administering said human antibody once every one to two weeks.

Dependent claims are further drawn to such methods, further comprising: (a) determining, after a period of at least one week following a respective last administration of said antibody but prior to a respective next administration of said antibody, the serum level of said antibody still present in the blood of said patient, thereby obtaining an intermediate serum level value for said antibody; (b) comparing said intermediate serum level value for said antibody with a predetermined serum trough level value for said antibody; and (c) effecting the respective next administration if the intermediate serum level value for said antibody is no more than 15%, preferably 10%, most preferably 5% above the serum trough level value or further comprising repeating steps (a) and (b) prior to step (c), or wherein the magnitude of the dose of said human antibody administered is set such that, at the end of the intervening time between two respective administrations, the amount of said human antibody persisting in the serum does not drop below the predetermined serum trough level, wherein said administering takes place once every two weeks, wherein said administering takes place once every two weeks and wherein the administered dose of said human antibody remains unchanged from one administration to the next, wherein the magnitude of the initial and all subsequent doses is determined by pharmacokinetic simulation and wherein said administering is intravenous, intraperitoneal, subcutaneous, intramuscular, topical or intradermal administration.

Kufer et al teach a human IgG1 antibody designated "H79" which comprises a heavy chain with the amino acid sequence of SEQ ID NO: 1 and a light chain with the amino acid sequence of SEQ ID NO: 2. This antibody has also been designated HD69, MT201 and adecatumumab in the art (see footnote[1]-also for the sake of clarity this antibody will be referred to the MT201 antibody in the rest of the action). Furthermore, as acknowledged by Applicant in the response filed May 26, 2009 at page 10, the MT201 antibody comprises the amino acid sequence of SEQ ID NO: 1 and the amino acid sequence of SEQ ID NO: 2. Kufer et al also teach methods of administering said MT201 antibody to human patients with a cancer expressing EpCAM by intravenous, intraperitoneal, subcutaneous, intramuscular, topical or intradermal administration and that the antibody is suitable for repeated in vivo administration at a suitable dose (see entire document, e.g., abstract and pages 1, 2, 12, 15 and 17). While, Kufer et al does not point to particular cancers in the genus of cancers to be treated, Kufer et al teaches that a murine monoclonal antibody 17-1A that binds human EpCAM was known to treat human colon or colorectal cancer as well as teaching that the MT201 antibody can bind to human colon carcinoma cells (see e.g., 2 and 23). Furthermore, this deficiency is made up for in the teachings of Naundorf et al and Raum et al. Naundorf et al teach that the MT201 antibody is effective in treating a mouse xenograft model of colon cancer derived from the human carcinoma cell line HT-29 that expresses EpCAM and that the antibody was administered on days 1, 4 an 7 (see entire document, e.g., abstract). Raum et al teach that the murine monoclonal antibody designated 17-1A that binds human EpCAM was known to treat human colon or colorectal cancer, and that the H79 antibody, now designated HD69 in this reference (see footnote), closely resembles the binding properties of the murine antibody, but that this antibody displays better

[1]The antibody comprising a heavy chain with the amino acid sequence of SEQ ID NO: 1 and a light chain with the amino acid sequence of SEQ ID NO: 2 appears to have been designated H79, HD69, MT201 and adecatumumab in the art. For example, Oberneder (of record) evidences that adecutmamab has also been designated MT201 (see abstract). Then Naundorf (of record) teaches that the MT201 antibody has also been designated HD69 (see page 102, left column). Finally, Kufer et al (of record) teach a antibody designated H79 that comprises a 4.5 heavy chain and a k8 light chain with heavy chain and light chain variable sequences set forth in figures 6 and 7 that are these sequences are present in SEQ ID NO: 1 and a light chain with the amino acid sequence of SEQ ID NO: 2 (see also page 35-37), while Raum et al teach the same sequences for the antibody designated HD69 (see Figure 1 and page 145).

cytotoxic effector functions as compared to the 17-1A antibody 17-1A (see entire document, e.g., abstract, Table 1 and 146, right column to 147, left column).

Furthermore, while Kufer et al teaches the MT201 antibody can be used in treatment protocols with repeated in vivo administration of the antibody, Kufer et al, Raum et al and Naundorf et al do not expressly teach administering the antibody once every one to two weeks or the other dosing schedules of delivery. These deficiencies are made up for in the teachings of Korman et al, Wolf et al, Raun et al and Leyland-Jones.

Korman et al teach methods of administering human antibodies to patients and that dosage regimens should be adjusted to provide the desired response and that dosage regimens can change over time by the exigencies of the therapeutic situation and that selected dosage regimens depend upon a variety of pharmacokinetic factors including the activity of the particular compositions of the present invention employed, or the ester, salt or amide thereof, the route of administration, the time of administration, the rate of excretion of the particular compound being employed, the duration of the treatment, other drugs, compounds and/or materials used in combination with the particular compositions employed, the age, sex, weight, condition, general health and prior medical history of the patient being treated, and dosages need to be titrated to optimize safety and efficacy. Korman also teach that the administration of the antibody can be weekly or once every two weeks and that human antibodies have a long half life (see entire document e.g., pages 19 and 20).

Wolf et al teach that the MT201 antibody has a half-life of several weeks and is in clinical Phase I/II trials in humans for treating cancers that express EpCAM(see entire document, e.g., pages s25 and S27).

Raun et al teach a human engineered antibody that binds EPCAM which is administered to a mouse xenograft model for colon cancer either once weekly or twice weekly to treat the cancer (see entire document, e.g., page 490, paragraph bridging the columns and page 491, Table 1)

Leyland-Jones (see entire document) teach that antibody pharmacokinetic simulations used to establish dose schedules for therapeutic antibodies, predetermined serum trough levels and dose schedules for the respective next administration to maintain a minimum serum trough level of antibody are known in the art.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to administer to human colon cancer patients the human MT201 antibody that specifically binds to human EpCAM once every one to two weeks and wherein the methods further comprise the various dosing schedules set forth in the claims. Notably, one of skill in the art would have been motivated to administer such antibodies to humans with colon cancer every one to two weeks because EpCAM antibodies were known in the art to be effective at targeting and killing colon cancer cells which would treat the cancer expressing EpCAM, the MT201 antibody was known to target and kill colon cancer cells to treat human colon cancer in a mouse model and the antibody was known to have a half-life of several weeks.

In this case, while the prior art MT201 antibody was at a relatively new stage of development so that further clinical data was not yet available, it is clear that the prior art taught how to obtain clinical data as evidenced by the references and one of skill in the art would have motivated to obtain that data in order to treat humans. Furthermore, the MT201 antibody was in clinical trials and was known to have a half-life of several weeks, so it is submitted that administering the antibody every one to two weeks was *prima facie* obvious as the frequency of antibody administration can correlate with the half-life of the antibody (see e.g., Leyland-Jones that estimated a half-life of 18-27 days for the particular antibody administered in their studies and administered that antibody every 21 days) and because Korman et al teach that human antibodies with long half-lives can be administered by once weekly or every other week dosing schedules.

Furthermore, as evidenced by Korman et al, many pharmacokinetic factors affect the dosage regimen for any particular patient, dosage regimens should be adjusted to provide the desired response and dosage regimens can change over time by the exigencies of the therapeutic situation, so it is further submitted that absent a showing

of unexpected results that the claimed methods of treatment would be considered to be obvious by one of ordinary skill in the art in treating cancer patients with anti-cancer antibodies as they would have predictably expected the claimed antibody to be effective to some extent to treat colon cancer when administered at some dose every one to two weeks based on its half-life. Notably, the Naundorf et al, Raum et al and Raun et al references evidence that multiple EPCAM antibodies were known in the art and that dosing schedules included administration three times a week, twice a week, weekly and monthly, so it is apparent that depending on the patient and the amount administered many different administration time frames would be effective when administering the MT201 antibody.

Notably, the MT201 antibody was known in the art as a therapeutic antibody which can treat colon cancer, i.e., the antibody was known in the art as a variable which achieves a recognized result and as set forth in MPEP 2144.05: "A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977).

In this case, the prior art of Kufer et al, Raum et al, Naundorf et al and Wolf et al evidence that the human MT201 antibody was cytotoxic to human colon cancer, and that the antibody had advantageous properties such as longer serum half-life, improved cytotoxic effector functions and immunogenicity as compared to a murine antibody that binds the human EpCAM antigen which can treat colon cancer patients, so one of skill in the art would have clearly recognized that the MT201 antibody would treat colon cancer and that the MT201 antibody was a result effective variable for treating colon cancer which could have workable or optimum dosing schedules determined by art known pharmacokinetic techniques so that the antibody could be predictably used in art known methods of treating colon cancer patients expressing the human EpCAM antigen. Therefore, one of skill in the art clearly would have been motivated to establish

a dose, schedule, and route of delivery that is both safe and effective, so as achieve a working therapeutic effect in treating colon cancer patients.

Secondly, as the half-life of the MT201 antibody was known to be several weeks and because one of skill in the art would have been motivated to monitor the half-life and other pharmacokinetic parameters in human patients undergoing treatment so as to provide effective cancer treatment, it is also submitted that one of skill in the art would have recognized that administering the antibody every one to two weeks would be a workable dosage schedule, i.e. a dosage schedule that would treat the cancer, as the schedule corresponds to the half-life of the antibody and the dose ***amount*** could be adjusted so that an amount that was effective to treat colon cancer could be administered every one to two weeks to maintain an effective serum amount of the MT201 antibody in the patient due to its long half-life. Notably, the claimed methods only recites that treatment occurs. There is no requirement on the amount of treatment or kind of treatment that needs to occur and there is no evidence of record that reasonably establishes that one of skill in the art would not have considered that administering the antibody every one to two weeks would be effective to treat colon cancer to some extent. In this case, in view of the evidence as a whole that the antibody had a long half-life and was effective to kill colon cancer, it is submitted that one of skill in the art would have reasonably expected success in treating colon cancer by administering the antibody every one to two weeks or by the other claimed parameters and one of skill in the art would have considered the claimed dosing parameters to be obvious variants of the prior are methods of treating colon cancer with the MT201 antibody as they would have been motivated to administer the antibody every one to two weeks based on its half-life of several weeks.

Furthermore, while this is a new ground of rejection, in the interests of compact prosecution, it is noted that inventor Dr. Prang-Richard has provided a declaration under 37 CFR 1.132 with statements regarding the establishment of dosing regimens for antibody therapy.

Notably, Dr. Prang-Richard states in points 8 and 9 of the declaration that:

“I also generally disagree with the examiner's statement that establishing a

particular dosing regimen for an antibody therapy is a matter of mere optimization" and that "While optimizing treatment regimens is always a desirable goal, it is quite unpredictable what regimens will provide improved results, if any".

In response, while the evidence and Dr. Prang-Richard's declaration has been considered as a whole, the declaration was not found persuasive with respect to the rejection set forth above. Notably, while Dr. Prang-Richard's opinion that establishing a particular dosing regimen for an antibody therapy is not a matter of mere optimization is noted, the evidence relied upon in this rejection establishes the MT201 antibody as a results effective variable for which workable and/or optimal conditions for treating colon cancer expressing EpCAM could be routinely determined by methods widely known in the art. Furthermore, while it is may be unpredictable what regimens will provide improved results, in this case the skilled artisan would be motivated to determine workable, i.e., effective regimens and it does not appear that it would have been unexpected that the claimed regimens would have been effective to treat colon cancer because the antibody was shown to be effective in a murine model and because it has a long half-life. Additionally, there is no evidence of record that the claimed methods of treating colon cancers using the MT201 antibody are any more effective than other methods of treating colon cancers using the MT201 antibody.

Then with respect to the Raum et al reference Dr. Prang-Richard states in points 6 an 7 of the declaration that:

"First, the properties of a mouse antibody to EpCAM (17-1A or Panorex® are not directly applicable to a human antibody against the same target (MT201).

Second, the murine antibody Panorex® of Riethmuller was provided to subjects using once a month administration regimen. Yet as is evident from FIG. 18, Example IV.4. of Kufer, MT201 (a.k.a. H79) shows much higher cytotoxic activity than Panorex®. Further, Raum discloses the beneficial properties of MT201, namely, a long in vivo half-life and minimal immunogenicity, and confirms the differences between MT201 and the 17-1A antibody of Riethmuller in cytotoxic activity (see page 146, right column second paragraph and Figure 5). One of skill in the art would not seek to increase the frequency of administration of MT201 over that of Panorex® when the former had a higher

cytotoxic activity as compared to the latter. Rather, one of skill in the art would choose a less frequent administration schedule for MT201, quite the opposite of what is now claimed."

In response, these arguments were not found persuasive with respect to the rejection set forth above because the Examiner has not been arguing that the properties of a mouse antibody are directly applicable to a human antibody. The Examiner recognizes that every particular antibody that binds EpCAM has different properties, but the question here is whether one of skill in the art would have found that administering the MT201 every one to two weeks to treat colon cancer to be obvious in view of the prior art. In this case the prior art evidences that antibodies, including EpCAM antibodies can be effective when administered at schedules more frequently than once a week, once a week, once every two weeks and less frequently than once every two weeks. Once again, the administration needs to only provide some minimal amount of treatment and as evidenced by the references, once an effective treatment is known in the art, one of skill in the art could administer the antibody once every one to two weeks to effect some amount of treatment of colon cancer.

Furthermore, it is unclear on what evidence Dr. Prang-Richard submits that "[o]ne of skill in the art would not seek to increase the frequency of administration of MT201 over that of Panorex® when the former had a higher cytotoxic activity as compared to the latter. Rather, one of skill in the art would choose a less frequent administration schedule for MT201, quite the opposite of what is now claimed", especially since point 6 states that "the properties of a mouse antibody to EpCAM (17-1A or Panorex® are not directly applicable to a human antibody against the same target (MT201)".

As evidenced by the references and in particular the Korman et al reference, many factors influence the amount and frequency of administration of any antibody in a given patient, so it is apparent that one of skill in the art would not base frequency of administration only on a comparison of two antibodies in an in vitro antibody cytotoxicity assay. Notably, as the MT201 antibody is a human antibody which would have reduced immunogenicity in humans as compared to the murine antibody, while the Panorex®

antibody is a murine antibody that was known to cause a human anti-murine antibody (HAMA) response. Furthermore, in the Riethmuller reference (JCO 5:1788-1794, reference C9, IDS filed 5/29/07) referred to by Dr. Prang-Richard, the researchers state that the dosing of the antibody was influenced by their being "afraid of a strong anaphylactic response to repeated administration of murine immunoglobulin" (see page 1793). Accordingly, as the MT201 antibody is a human antibody and such a strong anaphylactic response would not be expected in humans, one of skill in the art would not have been deterred from administering the MT201 antibody more frequently than the murine antibody.

Additionally, Applicant presents arguments in the response filed November 17, 2009 with respect to result effective variables. Notably, Applicant argues that "[t]aken to its logical conclusion, if dosing regimens are "result effective variables," then no dosing regimen would ever be patentable" and that while determining dosage parameters for administering the MT201 antibody may be desirable this does not make the claimed methods obvious.

In response, the prior art evidence as a whole needs to be examined to determine if a variable is a result effective variable and in this case the prior art taught that the MT201 was an antibody that could target and treat human colon cancers expressing EpCAM. Secondly, the examiner is not arguing that no dosing regimen would ever be patentable. Indeed if persuasive evidence of unexpected results for a particular dosage amount administered by a particular regimen that treats a specific cancer expressing EpCAM were provided then it might be established that *claims drawn to such methods* were patentable. However, the claimed methods recite treatment with any amount of antibody administered anytime every one to two weeks and no evidence commensurate with the broadly claimed methods has been presented to establish any unexpected results for the currently *claimed methods*. Additionally, the human antibody was known to have a long half-life of several weeks, methods of administering human antibodies weekly or every two weeks were known in the art and based on the teachings in the prior art, one of skill in the art would have expected that administering the MT201 antibody weekly or every two weeks at some dose and by the other claimed

methods would be effective to treat colon cancer.

Therefore, after considering the record as a whole, the claimed methods were *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

12. No claim is allowed.

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Strober et al (US Patent 5,853,697, 1998) teach that when administering antibodies to a human that one skilled in the art realizes that dosages are best optimized by the practicing physician and methods for determining dosages are described in the art (see column 3). Tokuda et al (BJC 8:1419-1425, 1999) teach that antibody pharmacokinetic simulations used to establish dose schedules for therapeutic antibodies, predetermined serum trough levels and dose schedules for the respective next administration to maintain a minimum serum trough level of antibody are known in the art.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brad Duffy whose telephone number is (571) 272-9935. The examiner can normally be reached on Monday through Thursday, 6:15 AM to 4:45 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Misook Yu can be reached on (571) 272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully,
Brad Duffy
571-272-9935

/bd/
Examiner, Art Unit 1643
March 9, 2011

/Misook Yu/
Supervisory Patent Examiner, Art Unit 1642